

ternal condyle was persistent for nearly a month. The patient was discharged, cured, August 14, 1894, with a fair motion in the knee-joint.

CASE V.—Louis S., aged fifteen years, was admitted to the wards of the Episcopal Hospital, June 14th. While hanging on to the back of a wagon the leg became entangled in a revolving wheel. On admission there were effusion into the knee-joint and marked softening over the internal condyle. Crepitus of a moist character could be detected, although with slight displacement. Extension with weight and firm lateral support, with bran-bags and long lateral splints, were employed. The patient made a good recovery, and left the hospital, cured, in fifty-seven days. The mobility of the joint was unimpaired.

A CONTRIBUTION TO THE PATHOLOGY AND MORBID ANATOMY OF AMYOTROPHIC LATERAL SCLEROSIS;

WITH A REPORT OF TWO CASES WITH AUTOPSY, IN ONE OF WHICH,
OBSERVED BY DR. C. L. DANA, A TERMINAL TUBERCULAR
CERVICAL MYELITIS AND PERFORATING NECROSIS
OF THE DORSAL CORD WERE FOUND.

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THE clinical picture which is called up by the name amyotrophic lateral sclerosis is a well-defined one, and, as clinical pictures go, is not subject to remarkable variations. So much cannot be said for the pathological process upon which the disease is dependent, nor for the morbid anatomical conditions found at the termination of the disease. The typical clinical manifestations of the disease have been found associated with changes confined to the anterior horns and no involvement of the lateral columns (Senator, *Wiener med. Wochenschrift*, November 31, 1894), and with degeneration of the entire motor tract, the primary and the secondary neuron (Kahler and Pick, *Vierteljahrsschr. f. pract. heilk.*, 1879; Kojewnikoff, *Archiv de Neurol.*, vol. vi., 1883; Charcot and Marie, *Archiv de Neurol.*, July, 1883; Lombroso, *Lo Sperimentale*, 1888; Lenaxalem, *Archiv de Neurol.*, vol. viii., 1887; Mott, *Brain*, "Spring," 1895). Again, cases have been observed in which anatomical investigation has shown degeneration of the motor and sensory systems. Hektoen has recently reported a case of this kind, a typical case of amyotrophic lateral sclerosis, with bulbar paralysis and a posterior sclerosis. Marie found degeneration in the columns of Goll (*Traite de Méd.*, vol. vi. p. 340); Oppenheim found degeneration in Burdach's column (*Archiv f. Psych.*, xxiv. p. 758); Charcot and Marie (*Archiv de Neurol.*, vol. x., 1885) have described degeneration in the columns of Goll; while Mæli found degener-

ation in the column of Burdach (*Archiv f. Psych.*, vol. x., 1880). It is thus seen that the morbid changes are not very constant.

The common pathological findings are destruction of cells in the posterior area of the medulla and the anterior cornu of the cord, and a degeneration of the pyramidal tracts; but with these conditions there is considerable variation, particularly in respect to the condition of the anterior nerves of the spinal cord, their terminations at the periphery, and the condition of the cranial nerves. It is in accordance with our knowledge of secondary degeneration and our conception of the anatomical and physiological unit, the neuron, to believe that when the anterior horn cells are diseased that the anterior roots will suffer in proportion and in intensity. But cases of amyotrophic lateral sclerosis have been described in which the anterior horn cells have been diseased and the anterior root and motor spinal nerves found intact (Kronthal, *Neurolog. Centralb.*, p. 130, 1891), while in the same case the cranial nerves arising from diseased nuclei showed well-marked degeneration.

Other cases of typical amyotrophic sclerosis (clinically) have been found associated with the lesions of poliomyelitis anterioris chronica (Oppenheim, *Archiv f. Psych.*, vol. xxiv. p. 758), with atrophy of the ganglion-cells in the anterior horns, arterial and venous hyperæmia, multiple hemorrhages, and incipient syringomyelia (Wolf, *Zeitschrift f. klin. Med.*, vol. xxv.), not to mention those cases which were shown on autopsy to have been due to internal hydrocephalus and tumor of the cord and cerebellum (R. Schultze, *Archiv f. klin. Med.*, vol. xxiii.), nor those of Kahler and of Schultze in which the symptoms of amyotrophic lateral sclerosis were found associated with gliosis.

The most casual reference to the literature of this subject will show the need for careful study of the morbid anatomy of this disease in order that safe inferences may be drawn as to the most constant pathological pathways that lead up to the diseased tissues of the body. Such study will expose not alone the nature of the disease, but eventually the cause as well.

As well known, therefore, as the disease is clinically, there are still many points in its pathogenesis which are very obscure, while the etiology of the disease is as yet absolutely unknown. The disease is much more uncommon than is generally supposed, if we may come to such a conclusion from the scarcity of well-authenticated cases with the pathological findings which have been published; the writer having been able to find but seventy-two such cases in an extended search through the literature. It behooves us, therefore, when opportunity is given to us for the study of this disease, before and after the death of the patient, to do so with as much care as possible, and particularly by the employment of those means and methods which have done so much in latter years to unfold or reveal the structural secrets of the nervous system.

As to whether the disease is a form of progressive muscular atrophy, as is held by Gowers, Leyden, and some others, or whether the primary lesion is a degeneration of the pyramidal tract and secondary involvement of the gray matter, as was suggested by Charcot and believed by many neurologists, is a question that will be settled when a sufficiently large number of cases which have been verified by histological study shall have been recorded.

It is with the hope of contributing something in this direction to the pathologico-anatomical basis of the disease that the two following cases are added to the literature. In both of them the course of the disease was rather rapid, after a somewhat abrupt onset, the clinical manifestations well pronounced, and some of the pathological changes found in the nervous system of a nature and degree which are uncommon. The first case was under my observation in the Hospital for Nervous Diseases, from shortly after the onset of the disease until death, a period of less than two years, and there was not lacking opportunity, therefore, to observe carefully the evolution and course of the disease. The second case, which I had opportunity of seeing at Prof. Dana's clinic at the Post-Graduate Medical School, was under the continual observation of Dr. Dana, who made a careful histological study of the diseased nervous system and then placed the material at my disposal. It is a pleasure for me to avail myself of the opportunity to express my obligations to Dr. Dana for so doing and for assistance in many other ways, and to Dr. George R. Elliott for assisting with the pathological specimens of the second case.

The clinical history of the first case is as follows :

M. S., aged thirty-three years, born in Russia, by occupation a gold-beater and maker of jewelry, entered the Hospital for Nervous Diseases November, 1894. When he came to the hospital he said that seven weeks before he began to have severe pain in the back of the head and neck, which radiated down to the shoulders, and which was accompanied by a feeling of stiffness in the neck. He became weak progressively, and particularly the right upper extremity began to lose its strength. His wife, who was seen later, makes addition to this statement by saying that he has not been entirely well for some time past, and that the first symptom was loss of dexterity and reliability of grip in the forefinger and thumb of the right hand. Then a year ago, or thereabouts, he began to complain of pain in the back of the head and neck. The gradually increasing weakness in the right hand hindered him from earning his customary wages; and instead of being content with this, or taking a rest, he applied himself without intermission and worked late every night. In fact, overwork is the only element that can be attributed as an etiological factor.

On inquiry into the family history nothing of importance was determined but that his mother had died of consumption. There is no neuropathic taint in the family. He is married and the father of six children, one of which died when eight months old; another, one of twins,

died at birth. He denies all forms of venereal disease, likewise excesses of any kind except smoking. For several years he had smoked cigarettes in great numbers and had inhaled the smoke. He does not remember to have had any severe illness since childhood. The family lived in three small rooms, and the food and hygienic surroundings were about as bad as they could be.

Shortly after the headache and pain in the neck set in he noticed a change in the voice; it became distinctly nasal, and this progressed gradually, so that when first seen there was a most marked twang with the dysarthria; and prolonged efforts at speaking exhausted him, as all the muscles of the face and neck were used to help bring the words out. In addition he had had a great deal of difficulty in swallowing, but this had gradually got better and when he first came under observation he could swallow fairly well. He did not complain of distress in the præcordium nor of cardiac palpitation, nor of any affection of the bowels, bladder, or sexual organs. There was no complaint of difficulty of vision, but for some weeks before coming to the hospital he had suffered a considerable vertigo.

Examination. The patient is a tall, sparely built, moderately anæmic and poorly nourished individual. He lies in bed, but can rise to a sitting position, and if given time enough he can get up, slowly and laboriously. The face is masked, expressionless, and staring. When the arms are extended there is considerable coarse tremor of the hands and fingers. The upper extremities are in a semiflexed position. When asked to extend the hands the attempted movements are slow, the little finger becomes extended, the third and fourth remain considerably flexed, and the index very much more so. There is inability to abduct any of the fingers except the little one. There is marked atrophy of the thenar and hypothenar eminences, and when these eminences are squeezed the patient complains of pain. Atrophy of the first interosseous space is pronounced. Passive movement of the arms is resisted, and causes increase of muscular rigidity. When asked to extend the fingers of the left hand it is seen that all the fingers can be extended except the third, although the others are not brought into complete extension.

There is atrophy of the thenar and hypothenar eminences as in the other hand, but the atrophy is not quite so far advanced. The joints of the wrist, elbow, and shoulder feel stiff and immobile. He is able to raise the arms from the side, but the movements are done slowly. Flexion of the elbow is more powerful than extension. There are marked spontaneous and stimulatable fibrillary muscular twitchings of both upper extremities, and this is particularly manifest in the arms. On tapping the belly of any of the arm-muscles the twitching which results is quick and sharp. The tendon-reflexes of the upper extremities are greatly exaggerated, and tapping the trapezii at their junction causes a quick movement of both elbows from the side. A light tap on the chin when the mouth is partly opened causes a striking reflex of the jaw and a shaking of the entire head. There is not much atrophy of the shoulders except that commensurate with the general wasting. There is conspicuous fibrillary twitching, and the mechanical irritability of all the muscles of the upper extremities is increased, particularly in the scapular muscles. The atrophy of the muscles of the extensors of the forearm is very striking. There is but little atrophy of the muscles of the lower extremities, so that they present a marked contrast to the

upper extremities. The lower extremities are spastic, the knee-jerks are enormously exaggerated, and the jerk is accompanied by a slight clonus. Ankle-clonus well marked. Patient complains of tenderness and pain when the lower extremities, especially the calves, are pressed. The gait is spastic in the extreme; when he attempts to walk he gets the heel off the floor, then the foot shoots forward quickly without the toe being raised. He cannot walk unless supported by the arms or from behind.

When he attempts to walk there is clonus when he gets the heel of one foot off the ground and starts to make a step. The right foot is more spastic than the left. When he attempts to stand he takes the position of a wooden man; there is no elasticity or grace about his station.

Examination of the sensibility shows marked hyperæsthesia of the lower extremities over the entire surface. The slightest touch with the point of a pin, he says, is painful. Contact, even the slightest, is felt with the greatest acuity. Extremes of temperature are detected with great rapidity. No loss of the sense of position. Great tenderness over the muscles of the lower extremities, the patient complaining bitterly when the calves or thighs are squeezed gently. There is considerable immobility of the head; when the patient attempts to turn the head the whole body turns too. Nodding movements are less limited, but done slowly. Face mask-like and immobile. For some weeks before he came into the hospital, he says he had difficulty in opening his mouth, and for a time it was barely possible to open it far enough to enable him to take liquid food; at the first examination it could be opened to about its normal extent. The buccal cavity is filled with tenacious mucus which the patient makes no effort to get rid of. The reflexes of the palate and pharynx are present, but not lively. The soft palate is raised on efforts of phonation. Sensibility of the pharynx and larynx seems to be blunted, but it is not lost. Inability to pucker the lips so as to whistle and likewise inability to smoke. It makes his face and jaws very tired to masticate, and he avoids solid food because after trying to chew it his jaw-muscles ache. There is no trouble in swallowing except that the movements of swallowing are performed very slowly. He can bulge out both cheeks and can wink both eyes. Movements of the eyeballs are normal. The pupils contract to light and to accommodation. Hearing, smell, and taste are found to be entirely normal. The tongue can be protruded and comes directly out; it has no appearance of atrophy, but it is a bit unwieldy, and it is liable, he says, to get caught between the teeth. There is no atrophy of the muscles of the face, yet when asked to wrinkle the forehead, show the teeth, etc., all these face-movements are done very slowly. Electrical examination shows response to the faradic current in all the atrophied muscles as well as in those not atrophied. In the thenar and hypothenar eminences there is reaction of degeneration. In the atrophied muscles the electrical irritability is quantitatively diminished both to the direct and the induced currents. The seventh and twelfth nerves and the muscle supplied by them respond to the electric currents. A noteworthy feature brought out in the first and other examinations was that a faradic current so strong as to be painful to the ordinary individual was very agreeable to the patient. The visceral organs seem normal and there are no vasomotor symptoms worthy of mention, except that the pulse remains rapid, about 100. Respirations are normal. Mentally the

patient is cheerful and hopeful. There is no disturbance of the bladder or of the bowels except that these functions, especially the latter, are discharged slowly and the patient has very little bearing-down strength.

The patient grew worse gradually, his symptoms being accentuated seemingly from day to day. Four months after his entrance into the hospital he is almost helpless. He tries to walk aided by two of the other patients, but on account of the spasticity, the weakness and tremor of the legs, he is unable to do so. The atrophy of the hands and of the forearms has progressed, and now it can be seen that the shoulder-muscles are becoming atrophic, the right more than the left. The hands have gradually assumed a contracted, semi-claw shape, and their dexterity is completely lost. The same condition of electrical and sensory irritability exists as when he first entered the hospital. The patient's speech is slow, drawling, non-inflected, and extremely nasal. The face still keeps the same masked appearance, and retains it very largely, even when the patient laughs, except the upper part of the face. Involuntary and uncontrollable waves of smiles and laughter pass over his face at times. He has great difficulty in opening the mouth beyond a very small amount on account of the tension of the muscles of the jaw. The neck is stiff and the head cannot be turned from side to side without turning the entire body. The tendon-jerks all over the body are extremely exaggerated. Pulse 105, irritable and accentuated by slight attempts at exertion. Respirations become labored and rapid on slight exertion. No visceral or sphincteric difficulty. Still has sexual desire and occasional pollutions. The musculature of the lower extremities is fairly well preserved. Mentally he is hopeful, very rarely cast down, and looks forward to recovery.

March 21, 1894. The atrophy has progressed so far in the muscles of the shoulder that it is impossible for him to raise the arms from the side to a perpendicular position with the sitting body. The hands are very much deformed as the result of the atrophy, the dexterity and grip of the hands are entirely lost, and the patient is absolutely incapable of helping himself in any way. The neck is still stiff, and as he lies in bed the impression one gets from looking at him or examining him is that he is completely rigid or "wooden." The reflexes, superficial and deep, are enormously exaggerated. There is now no pain in the head or neck. Sensorium entirely free, except that he is mildly hyperæsthetic to all forms of sensory stimulation. Pulse 110; respirations weak and more diaphragmatic than intercostal. Tongue unwieldy, but not at all atrophic, and still responds well to electrical stimulation. He can swallow, but it is a slow and laborious process; but fluids do not regurgitate. Speech the same as at the last examination, with the addition that it is more difficult to understand any of his words, and it is absolutely impossible for him to articulate the labials. No real anæsthesia of the fauces, pharynx, or larynx, but the sensibility of these parts is not very acute. The sphincters remain normal. Vision and hearing normal. Mentally the patient is painfully cheerful and often makes attempts at laughing, in addition to the involuntary waves of laughter, but they are toneless. The lower extremities are now seen to be undergoing an atrophic process in certain places, particularly in the peroneal and internal and femoral groups of muscles. The strength of the lower extremities, which has heretofore been quite well preserved, but which had been rendered useless on account of the severe rigidity, now became seriously impaired.

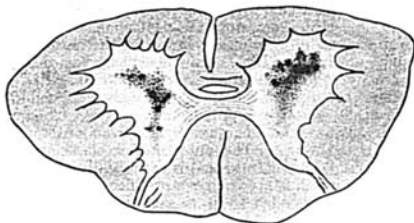
In the atrophied muscles of the lower extremities there was at no time reaction of degeneration, merely quantitative diminution of faradic irritability. The marked insensitiveness of the patient, previously mentioned, to a faradic current of great intensity was still apparent, and likewise the tenderness on pressure of the muscles.

The patient was not seen for six months from the date of the last examination, when on resuming my service at the hospital he was found to be completely bedridden and evidently in a most advanced stage of the disease. The bulbar symptoms had increased; his attempts at speech were powerless. A question would call forth an endeavor at articulation, but a slight opening of the mouth was followed by an increase of the tension of the muscles of the lower part of the face and neck, and, indeed, of the whole body, as the only result of the effort. The tongue could still be protruded beyond the teeth, and to the sight it did not appear atrophic; to the touch, however, it felt soft and pulpy. Swallowing was a tedious procedure, as fluids would escape through the lips after having been put in the mouth; solids could not be masticated, and even when taken in small bits they went down with painful slowness. There was no regurgitation through the nose. There was no real anæsthesia of the palato-pharyngeal region. The pulse was rapid and feeble; the respirations shallow and powerless, particularly deficient in intercostal action, and the most forced voluntary abdominal contraction was feeble. Efforts at coughing were futile. The only voluntary movements left in the upper extremities was a slight abduction of the arms. The anterior and interior femoral and the peroneal muscles had suffered most of the lower extremities. The reflexes are, as before, greatly exaggerated; a slight tap on the muscles of the back of the neck draws the head back with a quick jerk. The atrophy and deformity of the upper extremities had seemingly become as great as possible, and in the latter part of October the patient seemed suddenly to go to pieces, respirations began to be somewhat impeded, efforts at coughing were extremely exhausting, and soon a distressingly typical picture of failing heart and coexisting pulmonary oedema developed, and the patient quickly succumbed.

The autopsy made a few hours after death by my house-physician, Dr. Deady, revealed the cause of death to have been an apparently recent consolidation of the right lung and extensive pulmonary oedema. I shall confine myself to extracts from the post-mortem records which bear on the nervous system. The skull is not abnormal; the sinuses and vessels are overfilled; the pia is of normal thickness and shows a venous congestion; it is not adherent, and the convolutions and fissures of the hemispheres have a natural appearance. Particular observation was made of the condition of the paracentral region, but there was nothing to suggest any abnormality. The vessels at the base of the brain look and feel degenerated. The hypoglossal nerves look small and thin, and likewise do the anterior roots of the spinal nerves, especially those of the cervical region. Aside from this the cord looks normal to the naked eye, until it is cut across. When a transverse section is made in the mid-cervical region it is seen that the anterior horns are of a dark reddish-brown color and of very much impaired consistency; while they are not absolutely liquid, they are extremely pulpy. An attempt to show this appearance is made by Fig. 1. On further cross-section of the cord preparatory to hardening, it was found that this remarkable

condition of the anterior horns was limited to the cervical region from about the second to the sixth segments. The discoloration did not give the appearance of an acute hemorrhage, but rather reminded one of the appearance of the brain in that condition which is known as red softening.

FIG. 1.



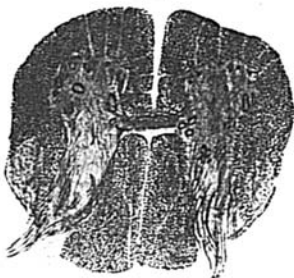
Small pieces taken from several of the atrophied muscles were of a pale-red appearance, flabby to the touch, and with the naked eye were seen to be very heavily striated with whitish-yellow lines and nearly devoid of muscular fibre.

The entire conducting pathway from the cortex to the periphery was prepared for microscopical examination. Small pieces from the paracentral cortex and from the cervical, dorsal, and lumbar levels of the spinal cord were placed at once in 96 per cent. alcohol, and later in absolute alcohol, for thirty-six hours, and then stained according to the methyl-blue method of Nissl. Other pieces from various levels of the cord, medulla, and internal capsule were put in Müller's fluid for eighteen days and then stained after the method of Marchi and Algeri by being put, without previous washing, in a mixture of two parts of Müller's fluid and one part of a 1 per cent. solution of osmic acid, in which they were allowed to remain one week. The remainder of the nervous system was hardened in Müller's fluid and studied later with the aid of many different stains, but particularly by the hæmatoxylin method of Weigert, and its modifications by Pal and Vassale, by Van Gieson's carmine-stain, and by nigrosine.

A description of the microscopical appearances of the cord taken from the different levels, cervical, dorsal, lumbar, and sacral, will be given here, and for the sake of convenience we will begin our description with the sacral region and go upward. Second sacral: The most striking features of the sacral region are, first, the excessive vascularization of the anterior horns; second, the degeneration of the pyramidal tracts, which, of course, at this level are comparatively small and close to the periphery of the cord; and third, the scantiness of cells in the anterior cornua. At this level, as indeed at all other levels of the cord at the junction of the anterior commissure with the base of the anterior horns on either side, are to be seen sections of bloodvessels cut across, their walls thickened and their spaces filled with blood. Throughout the anterior horns numerous circular spaces are to be seen; some of them are filled with blood, while others are entirely empty. With the high

power some of these spaces are seen to be places which were occupied by bloodvessels and from which the vessel has dropped, while others were formerly occupied by small ganglion-cells. Where the vessel still remains the thickness of the walls and their rigid, gaping appearance are striking. The direct pyramidal tracts are nearly, if not quite, entirely degenerated. Throughout a cross-section of this tract are scattered here and there nerve-fibres which are not degenerated, but they are surprisingly few and need a high power for their detection. The antero-lateral descending and ascending bundles seem to be quite normal. The anterior root-bundles look thin. Nissl's stain of sections from this level shows a massive atrophy and disappearance of cells, particularly of the mesial and dorso-lateral groups. Where these groups are to be found normally are seen a few cells, but they look old and decrepit. They are round, granular, and clumped, and their axis-cylinder and protoplasmic processes look like weaklings. The anterior and posterior commissural fibres seem normal. The central canal is entirely filled up with a homogeneous substance which is apparently a proliferation of the ependyma. The central canal is distended so as to cause a considerable bulging of the posterior commissure.

FIG. 2.



Relatively slight degenerative changes.

FIG. 3.



Cells in lumbar region.

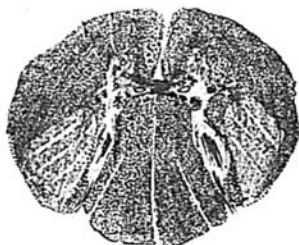
Second lumbar region: Complete degeneration of the lateral pyramidal tracts, and with the degeneration there is apparently a small amount of neuroglia-hyperplasia. All the other conducting pathways at this level seem normal. The central canal is filled up and bulging as in the sacral region. The evidences of excessive vascularity and vascular decay are quite as apparent as in the sacral region, but much less than in the dorsal and cervical region. (Fig. 2.) Marchi's stains of this level show the degeneration of the pyramids macroscopically. Microscopically the changes in the pyramids are best seen with this stain on longitudinal section (frontal). There are no changes in the sense of Marchi; i. e., the existence of numerous minute black granules and clumps in the course of fibre-bundles which are still undergoing the process of degeneration. In the specimens a few black granules are seen, but they are scattered around in the most irregular manner, and their presence must be regarded

as accidental or normal. One must conclude, therefore, that the degeneration of the pyramids had gone on to completeness before the death of the patient. Therefore the granula, which indicate a decaying process in the medullary sheaths, are not present. This stain shows likewise a slight thickening of the neuroglia on the periphery of the sections and especially at the periphery of the lateral parts.

Nissl's stain reveals a great scarcity of cells; in many sections only four or five cells can be found in an entire cornua, and these shrunken, with thin processes or without any; some even looking like a clump of color. In some of the cells the nucleus can be made out, and in all the nucleolus. All the atrophied cells stain very dark, and some of them are nearly homogeneously stained. In other sections from the lumbar enlargement a greater number of cells are found in some sections and a less number in others; all of them, however, seem degenerated. A drawing of a section showing the greatest number of cells, which is here given (Fig. 3), shows likewise the serious degenerative changes which the cells have undergone. It is seen that the chromophyllic granules are disintegrated and disseminated throughout the entire cell; the cell-body is deeply pigmented, and the pigment is not equally distributed, but clumped. In others the shape of the cell is altered, and its entire components, cell-body, axis-cylinder, and protoplasmic processes, seem to be in an advanced stage of disorganization.

The small cells found normally in the zone between the bases of the anterior and posterior horns do not seem to be quite so abundant as normal. The substantia gelatinosa and posterior roots are normal.

FIG. 4.



To show vascular and degenerative changes.

FIG. 5.



To show vascular and degenerative changes.

Second dorsal segment (Fig. 4): Weigert's stain shows almost total degeneration of the crossed pyramidal tracts. The direct pyramidal tracts are degenerated in a very much less degree. Clarke's column of cells shows clearly, and, as is afterward found with the methyl-blue stain, these cells are normal, save for a shrunken, clumped appearance in a few of the cells. At this level the excessive vascularization is more marked than in the lumbar region and less than in the cervical. Bloodvessels with thickened walls, some cut across, others cut obliquely, are seen in numbers greatly exceeding the normal, while here and there are seen the

spaces from which vessels have dropped, while other spaces indicate the place formerly occupied by ganglionic cells. Specimens stained after Nissl show a surprising poverty of cells, and those to be seen, with the exception of Clarke's column, are situated in the centre of an enlarged pericellular space and give a stunted appearance. The few cells that are to be seen are principally, at this level, in the dorso-lateral, the so-called group of the lateral horn, or antero-internal groups. In fact, most of the cells of the groups of the lateral horns appear normal and are but slightly diminished in number. Marchi sections reveal a condition absolutely analogous to that found in the lumbar region. At the base of the posterior horns normal cells are seen now and then. Such are also observed in the region corresponding to Bechterew's lateral group of the posterior horn (at the lateral border of the gray substance between the posterior and lateral horns).

Seventh cervical (Fig. 5): Hæmatoxylin stain, degeneration of the crossed and direct pyramidal tracts. The degeneration does not seem so complete or quite so extensive as in the dorsal region. That is, with a high power there is to be seen a greater proportion of nerve-fibres with moderately good medullated sheaths. Slight degeneration of the direct pyramidal tracts. The other conducting pathways of the cord seem normal. The condition of the anterior horns at this level, and above, is not an easy one to describe with accuracy.

The bloodvessels of the white and the gray matter, especially of the gray, show enormous alterations. One sees tortuosities, circumscribed and irregular dilatations, aneurismatic bulging out of a circumscribed part of the vessel-wall or cylindriciform dilatation, especially a part where a vessel divides. In most places the walls of the vessels are thickened, but in some places corresponding to the dilatations the walls are thinned. Numerous large and small foci are seen in the gray matter; these are formed by the accumulation of small cells. There is no doubt that these cells are not leucocytes, but red corpuscles, and that consequently we are dealing with small capillary hemorrhages. In one section the source of the hemorrhage can be distinctly traced.

One sees a bloodvessel enter a hemorrhagic focus, where it seems to end, but with a high power it is seen distinctly that the vessel is ruptured at this point. The hemorrhagic foci are numerous: several can be seen in one section and every few sections from a series shows some new ones. Aside from these hemorrhages a particular feature is the large number of spider-cells to be seen, especially near the border of the anterior horns. The spider-cells are more numerous here than in the other regions of the cord.

There would seem to be a decay of this region, a state of necrobiosis and necrocytosis. The condition of excessive vascularization is greater here than in any other region of the cord. In addition to this there would seem to be a rarefaction of the structural foundation of the anterior horns, a brittleness of it, and in many sections, cut with the greatest care from most carefully hardened and imbedded specimens, a fracture and dropping out of the substance. Here and there around the thickened and filled bloodvessels may be seen a corpuscle that is outside the vessel-wall, but a careful search did not find anything which in the widest stretch of the imagination could be called diapedesis.

Methyl-blue stains revealed the cells of this region to be in a bad condition. One is struck first by their scarcity and then by the smallness in

size and lonely appearance of those that are to be seen. Instead of groups of cells, which normally superimposed one above the other go to make up columns, we see here one or two shrunken cells with such stunted process that their ganglionic character can scarcely be recognized, and an irregular granular clumped appearance, situated in the centre of an excessively dilated pericellular space. The cells of Clarke's column alone seem normal.

The central canal is not so completely obliterated as in the dorsal region, but is filled up with a proliferation of the ependyma which causes it to bulge out posteriorly and gives it greatly increased outline and a somewhat crescentic shape.

The fibres going out to form the anterior root-nerves appear extremely small and delicate.

Stains by the Marchi method show the degeneration of the pyramidal tracts and the absence of the characteristic reaction indicates that the process of degeneration had become completed. A part of the right posterior column is lightly stained, but there is much reason to believe that this was the result of incomplete drenching of the specimen, which was a bit large, with the Müller's fluid and osmic acid.

As we ascend in the cervical cord we find nothing but what the description just given will not apply to and cover but the one fact, that as we go brainward there is to be seen a gradually increasing number of normal-appearing medullated fibres in the pyramidal tracts, so that by the time the beginning of the decussation (or the end, rather) is reached more than half the fibres are healthy-looking.

Transverse section of the medulla at a level of the lower extremity of the inferior olive shows that there is scarcely a cell in the hypoglossal nucleus. At this level, laterally and ventrad to the central canal, the large multipolar cells of the twelfth nerve nucleus should begin to show themselves very conspicuously in the normal specimen; but in this case, with the exception of two or three small stunted, black, granular-appearing cells, the space looks transparent and thin. The emerging trunk of the hypoglossal nerve seems, in specimens stained with hæmatoxylin, to be thin, narrow, and delicate. The nucleus of the eleventh nerve seems normal. The nucleus of the tenth nerve is seen, and the cells stained with carmine and examined with the immersion-lens look dark, pigmented, and with increased perinuclear and pericellular spaces. There is unquestionably a degenerative process in these cells. The fasciculus rotundus is present, and, although it is not impossible to say that it is diseased, it looks, in many specimens, a bit suspicious. The pyramids look quite normal. In fact, with the exception of the excessive vascularity of this part of the medulla, the sections seem to be otherwise normal. It is necessary to say, in this connection, that the vascular changes, although quite well marked in the medulla, were not nearly so advanced in degree nor so extensive as were those in the spinal cord, especially in the cervical region.

In the decussation of the pyramids the number of degenerated nerve-fibres to be seen was relatively small, but as soon as the level of the cervical cord was reached going downward when the pyramidal fibres had completely crossed the number of degenerated nerve-fibres to be found in each succeeding section became greater, so that when the fourth cervical segment was reached more than two-thirds of the pyramidal fibres, roughly estimated, would seem to be diseased.

Other important elements in the medulla at this level, including the decussation of the fillet (in which Kronthal found degenerative changes in a case of amyotrophic lateral sclerosis), the nucleus lateralis, and the gray substance of the funiculus gracilis, cuneatus, and substantia gelatinosa, seemed entirely normal.

Sections of the medulla at the middle of the olivary body show that the changes to be seen are confined to the posterior area of Flechsig. The hypoglossal nucleus can scarcely be found. Instead of the large rich nuclei divided into several parts, which should be seen at this level, there is but a cell here and there, and that looking like a vagrant. The emerging root of the twelfth nerve looks small and delicate. The small hypoglossal nucleus of Roller, which lies in the ventral part of the hypoglossal nucleus, seems, however, quite normal. (The contention of Forel that this small group of cells does not give origin to any of the fibres of the twelfth nerve would seem to receive some support from the findings of this case.) The nucleus of the tenth nerve, its two parts on the floor of the ventricle, seems normal; the nucleus ambiguus or vagal accessory nucleus is very indistinct and the cells in carmine look small and atrophic.

In a few sections at this level, which had been stained after the Vassale method, the cells of the olivary bodies looked small, atrophic, and with large pericellular spaces. Sections stained with the Weigert or Pal method did not show similar appearances, and it was concluded, therefore, that this appearance was due to the heat used to hasten the colorization in the Vassale; particularly as the olivary bodies have no connection with the spinal cord and were expected to be normal, as they were.

Transverse section of the uppermost limits of the medulla showed a striking feature, inasmuch as the apex of the hypoglossal nucleus was here to be seen with great distinctness. It is well known that the twelfth nerve nucleus ends at about this level and that it goes to its upward termination like the sharpened end of a wedge. It was this portion of the nucleus that now showed itself so distinctly in contrast to the degenerated, shrunken parts below. In serial sections going from below upward from the junction of the middle and upper parts of the medulla, the number of cells to be found in the hypoglossal nucleus was more apparent. So that it would seem that the part of the nucleus to suffer almost entire ablation was the lower one-half, and that above this the cells were but partly destroyed, but that a very large part.

The small-celled glossopharyngeal nucleus—that is, the upper part of the common accessorio-vago-glossopharyngeal nucleus—was easily to be made out in sections of the medulla at the middle of the restiform bodies. The large-celled glossopharyngeal nucleus is undoubtedly affected, although in nowise to be compared with the impairment of the twelfth nucleus. The cells are shrunken, their processes thin or blunted, and their pericellular spaces are enlarged. At the same time it is necessary to say that a large number of cells are to be seen which are apparently in a good condition.

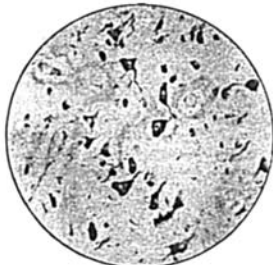
The eighth nerve, its nuclei and connections, and Deiter's nucleus are in a good state of preservation. A most careful examination was made of the nucleus of the facial nerve, and, although in some specimens of the upper medulla and lower pons the cells did not seem to be quite what they should be, taking it all together not sufficient and constant changes

were found in these nuclei to warrant us in saying that the cells were diseased.

The emerging root of the vagus was thin and the ascending root of the fifth entirely normal.

We may curtail our description by saying that from this point on to the cerebral hemispheres nothing showing a departure from the normal could be found. The pons, the mesencephalon, and the region of the internal capsule were most carefully studied in serial section, stained by the hæmatoxylin and carmine dyes, and nothing abnormal was found. Likewise the pieces which had been examined after the method of Marchi did not reveal any degeneration in these parts. In fact, it may be said that above the junction of the pons with the medulla the nervous system was found normal. Pieces of the cortex from the paracentral region studied by the aid of Nissl's stain show that the cells of the cortex appear in the highest degree normal. (Fig. 6.) A careful study of this region was made, not alone with the cortex taken from this patient, but side by side with pieces taken from a patient who had died of disease of the vegetative

FIG. 6.



Cortical cells. High power.

organs and in whom there never had been any cerebral trouble, and the cells of the cortex taken from the patient with amyotrophic lateral sclerosis, compared most favorably with those in the control-specimens. An examination of the pieces of the hypoglossal, ulnar, and popliteal nerves, which were stained with osmic acid, carmine, and hæmatoxylin, showed a degeneration of some of the nerve-fibres and a coexisting overgrowth of interstitial tissue. The degenerative process was more marked in the hypoglossal and ulnar than in the nerves taken from the lower extremities. The specimens stained with osmic acid showed the degeneration most strikingly by causing the degenerated fibres to take on a decidedly black appearance. The increase of interstitial tissue was not to be seen in each place where degenerated nerve-fibres were best made out; on the contrary, in several such places no proliferation of vulgar tissue could be seen at all. So that the impression which was received was that the atrophy of nerve-fibres was by no means a secondary one, using the word secondary here in the sense that the nerve-fibres were encroached upon by overgrowing and ingrowing connective tissue.

The striking feature in this case is, then, the change in the vascularity of the spinal cord and, to a less extent, of the medulla. Throughout the entire extent of the cord they are to be seen, but especially in the cervical and dorsal regions. The walls of the vessels are thickened, their calibre is large, except as encroached upon by proliferation of the tunica, and their lumen is filled with blood. The perivascular spaces are distended, and this particularly in the gray matter. The area of softening, if such it can be called, which was found and which was so conspicuous in the cord in its fresh state in the cervical region in the domain of the anterior horns, was due in part to the overdistended bloodvessels, and in part to the acute necrotic changes, necrobiotic, terminal phenomena which had antedated death for a short time, in all probability. There was no shrinkage of the size of the anterior horns and no marked variation from normal in their contour. The morbid anatomical conditions of the cord aside from this were those commonly found with this disease, viz., a degeneration of the crossed and direct pyramidal tracts and degeneration and atrophy of the ganglionic cells of the anterior horns with a degeneration of the anterior root-nerves and their continuation to the periphery.

The changes in the ganglionic cells of the anterior horns, the cytogenic changes, as determined by the Nissl stain, were of such a character as to leave no doubt of the intensity of the degeneration in those cells which had not been absolutely destroyed. The dissemination of the chromophyllic granules throughout the ganglionic cells has been shown to be entirely apart from changes incident to rest and fatigue. The absence of the small rods which are stained blue in the healthy cell with narrow unstained areas between them, and the uncertain differentiation between the nucleus and the nucleolus, all bespeak the intensity of the degenerative process in the ganglionic cells of the cord.

Clinical summary of Case I.: Male, aged thirty-three years; Russian; occupation gold-beater. Onset of symptoms nearly two years before death. First symptoms pain and stiffness back of head and neck; nasal, slow speech; weakness and loss of dexterity of fingers of the right hand; stiffness and immobility of muscles of face; later weakness of left hand; development of stiffness and weakness in the lower extremities and spastic gait. Normal condition of the sphincters and preservation of all the sensory functions, with hyperacuity of the sense of touch and diminution of acuity to the faradic current. Increasing rigidity of the upper extremities, with atrophy of the hand-muscles and later those of the forearm. Myotatic irritability enormously exaggerated; chin-reflex, occipital phenomenon, ankle-clonus, triceps-reflex, etc. Paresis, atrophy, and spasticity more marked on right side than on left. Quantitative loss of electrical irritability in atrophied muscles. In small muscles of hand reaction of degeneration. Masked appearance of face; waves of uncontrollable smiling and laughter. No apparent atrophy of face or tongue. Characteristic bulbar speech, unwieldiness of tongue, dysphagia, and slowness of swallowing. Tachycardia. Mentally bright and hopeful. Course of disease continually progressive; increasing stiffness and atrophy, especially of hands, forearms, and shoulders; increasing rigidity of head, neck, and, to a less extent, the face; spasticity of lower extremities enormous, becomes almost completely rigid. Bulbar symptoms increased in severity, tongue feels soft and flabby, mouth filled with tenacious mucus, swallowing becomes more difficult. Elec-

trical irritability has become gradually diminished, but complete reaction of degeneration only found in muscles of hands. Anarthria, aphonia; great tachycardia; physical restlessness; mentally uneasy; anxious; respirations shallow; rapid, ineffectual filling up of lungs; death, November, 1894.

Summary of morbid changes: In cervical portion of cord in fresh state, from third to sixth segments reddish, softened appearance in the area of anterior horns. Almost complete degeneration of crossed pyramidal tracts, from the medulla to the end of the cord. Degeneration in the uncrossed pyramidal tracts, but not so extensive or complete. Evidence of degenerated bloodvessels and excessive vascularization throughout the cord, especially in the cervical and dorsal regions and most evident in the gray matter. Massive atrophy of the ganglionic cells of the anterior horns throughout the cord, remarkably so in the cervical region, where they are almost entirely absent, and the few that are to be seen in a section are in a high state of degeneration. Increase of the spider-cells, particularly in the cervical region. Best preservation of cells of any individual column are the cells of the groups of the lateral horns. Central canal filled up and distended with a proliferation of the ependyma. Capillary hemorrhages in the cervical gray matter, associated with rarefaction of the ground-substance of the anterior horns, and a condition of necrobiosis. Striking degeneration of the twelfth nerve nucleus throughout its entire extent, except at its very termination ventrad. Slight degeneration in the common accessorio-vago-glossopharyngeal nucleus. Very slight degeneration in the nucleus of the tenth nerve. Nucleus of the seventh nerve apparently normal. No changes in the motorial pathway above the pons, and cortical cells of the motorial areas entirely normal. Atrophy of the trunks of the twelfth, the ulnar, etc., and degeneration to be seen microscopically. Usual changes in the muscle-fibres.

This case would seem to give testimony in favor of the view enunciated by Charcot, and in opposition to the views of Leyden, Gowers, Senator, and others, inasmuch as the Marchi method of examination showed that the degeneration in the crossed and uncrossed pyramidal tracts had reached its completion. Of course, it is impossible to say how long this antedated death. It is likewise probable from the clinical history that the spastic symptoms had preceded the trophic for some considerable time, the loss of dexterity and agility of the fingers, the stiffness of the neck and face muscles, and the dysarthria, being the first symptoms aside from the headache and vertigo. The symptoms of spasticity were likewise the first to reach their height, and that a considerable time before any evidences of muscle-atrophy were detected. As these symptoms were dependent upon the degeneration of the pyramidal columns, we can, at least, say with certainty that these were the first to be diseased and the first to reach destruction. That is, it is probable that the degeneration of the gray matter was secondary, or deuteropathic. It is such a view that Charcot took of these cases when they were first recognized, and which Erb has helped to establish. It has been difficult to furnish absolute proof of the truth of such a contention, but a case

which has recently been most carefully described by Strumpell will go a long way toward establishing it, by showing, first, that there is a primary systematic degeneration of the pyramidal tracts which causes a symptom-complex exactly similar to that of amyotrophic lateral sclerosis minus the atrophy alone (Strumpell: "Ueber einen Fall von primärer systematischer Degeneration," *Deutsche Zeitschr. f. Nervenheilk.*); and, secondly, that there were found on histological investigation certain conditions which would seem to indicate that the gray matter was becoming affected when the patient died. Strumpell regards his case as belonging to the type of amyotrophic lateral sclerosis, in which the degeneration is confined almost entirely to the pyramidal tracts, while the motor nuclei in the pons, the medulla, and in the anterior horns, as well as their peripheral prolongations, are in part not involved at all, while in part they are involved to a slight degree. The grounds for such a belief are substantiated, he thinks, by the fact that the disease occurred in an elderly man, who had previously been entirely well and in whom there was no inherited or acquired defect; and by the fact that the disease ran a rapid course, and that the first appearance of the disease was referable to the hypoglossal nucleus and the motor nuclei of the cervical cord, that is, in the very nuclei which first showed the manifestations of amyotrophic lateral sclerosis.

CASE II.—D. O'C., aged forty-eight years; England; pianomaker; married; was seen at Prof. Dana's clinic at the Post-Graduate Hospital in January, 1894. He was referred there by Dr. William H. Leszynsky, who furnished many clinical facts regarding the patient. The family history is negative; no nervous disease nor anything resembling the present illness being found in the ascendants. When a child he had scarlet fever, but no other disease. Eight years ago he had iritis in the left eye, and for several years had recurrences in the right eye. Has had gonorrhœa, but denies syphilis. No history of alcoholism. He is unable to give any history of lead-poisoning or of any severe muscular exertion. He states that the eye affected has always been weak. He has had flat-foot and some pains in the foot in consequence of it. Six years ago he injured the right foot so that walking has always been somewhat troublesome. In October, 1893, the patient first noticed a temporary difficulty and indistinctness of speech, and a little later he noticed a weakness in the left arm. This latter had gradually become worse. The speech-defect, which had entirely disappeared, came on temporarily a second time, and he did not recover so quickly from it, and after a few more recurrences the speech-trouble became permanent. This he dates at about December, 1893. About this time also he noticed that his legs were growing weaker, so that walking was more difficult. He observed a gradual atrophy along with the weakness in the left arm, dating as far back as November, 1893. The history, therefore, so far as could be obtained, shows that the first trouble noticed was that of articulation, but that the first permanent trouble was the weakness and atrophy in the left arm; the speech-trouble next became permanent, and then the leg-trouble. All three disturbances were present when seen in January,

1894. At that time, however, the speech-trouble was very slight, and the arm-trouble was by far the most prominent defect.

Examination at this time showed a normal mental condition and healthy thoracic and abdominal viscera. The general nutrition of the man was also good, and he was himself a large and rather strongly built individual. There was a partial paralysis of the muscles of the left arm, forearm, and shoulder. The hand-muscles were most affected, the arm- and shoulder-muscles next. He was unable to flex or extend the fingers, except very feebly. Adduction and abduction were also extremely weak. He could pronate, but could supinate only feebly. Flexion and extension of the forearm could be done with great difficulty, and the arm could be raised only a little way from the side. The shoulder-, arm-, forearm-, and hand-muscles all showed a decided atrophy, which, however, did not affect single physiological groups in the way usually seen in the Duchenne-Aran type of progressive muscular atrophy. There were no contractures. The muscular reactions were taken by Dr. Dana with much care about the latter part of January. They showed in the left deltoids sluggish reaction to the galvanic current, with equal or greater irritability to the positive pole. The galvanic irritability was, if anything, diminished. In the left biceps the cathode-contraction is greater than the anode, and the irritability diminished. In the forearm the flexor muscles showed on the left side a diminution of galvanic irritability with, at the same time, a cathode-closure tetanus. The extensors of the forearm showed cathode and anode tetanus and a slight diminution in galvanic irritability. There were no fibrillary contractions. The tendon-reflexes were greatly exaggerated. There were no sensory disturbances whatever. The patient suffered from no pains and had no anæsthesia either to touch or pain or temperature, nor was there any ataxia. There is some rigidity of the left shoulder, caused by contraction of the pectoralis major, and slight rigidity at the elbow, caused by contraction of the biceps. Both the legs were weak, the left being a little more so than the right; and some atrophic change was present, though not marked and not affecting any special groups. The patient could not get up from a chair without assistance, and in sitting down he dropped suddenly into his seat. When standing he assumed a stooping posture. (Fig. 7.) He was able to walk a short distance with some difficulty. The knee-jerks were greatly exaggerated and ankle-clonus was easily produced. There was also an increase in the plantar reflexes. There were no sensory disturbances in the legs or body. The patient had no trouble with the bladder, and had had none at any time, nor was there any disturbance with the rectum. His appetite was fairly good. He had no difficulty in swallowing at any time. His bowels were regular. The eyes were normal as regards the reflex of the pupils and the optic nerves and the movements of the eyeballs. There was no disturbance of the special senses of smell, taste, and hearing.

The patient was admitted to Dr. Dana's service in Bellevue Hospital, and was given iodide of potassium and electricity and at times hypodermic injections of strychnine. At one time he made some improvement, but after about two months he again grew weaker and his speech-defect became more marked. In addition to this he had certain peculiar spasmodic movements of the lips, tongue, and jaws, more particularly of the tongue. He would go through movements as though he were licking his lips, or chewing movements which appeared to be

almost voluntary, but which he distinctly stated were not under his control. His speech at no time was particularly affected, the articulations being simply a little muffled. He was able to pronounce consonants, and he did not even have what would be termed a syllabic speech. It

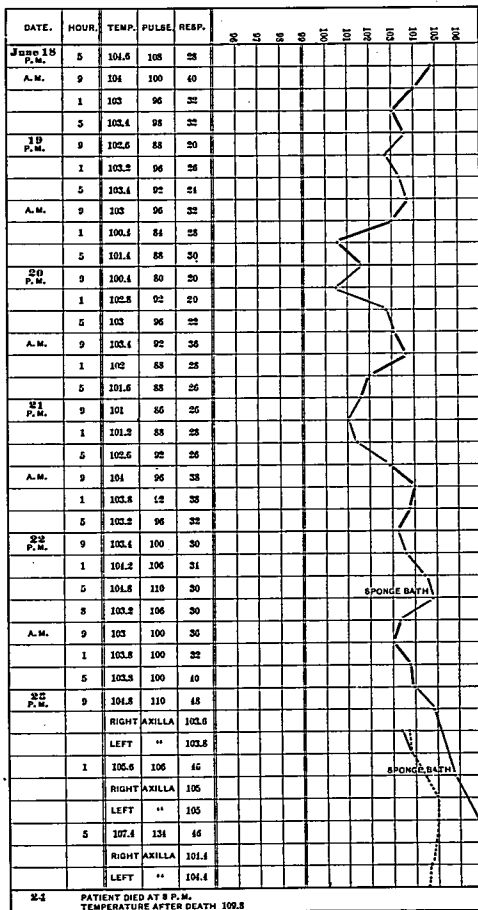
FIG. 7.



Showing patient's posture.

appeared as though his speech-disturbance was due more to stiffness and spasm in the tongue than to any actual paralysis. About June 15, 1894, the patient complained of chilliness and fever and about feeling extremely weak. He was obliged to go to bed, and there he remained until June 25th, when he died. During this time his temperature continued to range between 102° and 104° or 105° F. No definite cause could be found for this, the lungs remaining clear and he having no evidences of an inflammatory process anywhere. He suffered a little pain in the

FIG. 8.



back, especially in the lower part, but none in the arms or legs. The paralysis in the arm and the weakness in the legs increased, but there was no involvement of the sphincters. His mind continued clear, and he did not seem to suffer very much. In the last two days he became much weaker and the mind seemed a little clouded. During this time the house-physician, Dr. Watkins, tested his sensation in the legs and arm, and he informs me that there seemed to be some anesthesia at that time. The temperature on June 23d began to rise steadily until on the evening of June 24th it had reached 109.8° F., and he died at that time. The appended temperature-chart represents graphically the results of the infection on the temperature. During the last hours of his illness he was unable to speak or swallow.

The post-mortem was made by the senior assistant house-physician, Dr. Russell, and I (Dr. D.) am indebted to him for pains taken in this matter. The brain, spinal cord, the brachial plexus on the left side, and a part of the ulnar nerve of the left side were removed. The portion of the spinal cord reaching from about the third to the seventh cervical nerves was not obtained. The brain, to gross examination, seemed somewhat congested but otherwise normal, although upon the surface of the pia mater in the neighborhood of the Sylvian fissure a few granulations were seen. The spinal cord on section in the fresh state was found to be soft in the neighborhood of the upper dorsal region, and on cutting it down through the dorsal region a spot of white softening could be traced extending along through the posterior columns. This perforating softened area gradually grew smaller, ending in the neighborhood of the lumbar cord. It was perfectly white and showed no signs of hemorrhage, nor were there any evidences of exudation or inflammation about the dura or pia mater. Section through the pons and medulla showed no apparent lesion. The tissues, however, were placed without extended examination in a solution of Müller's fluid and were then transferred to a 4 per cent. solution of bichromate of potash. The piece of the cord at the upper dorsal region was placed in alcohol for bacteriological examination. The pieces of cord which had been placed in alcohol and later subjected to bacteriological examination revealed the presence of tubercle-bacilli.

The methods of staining employed in this case were the hæmatoxylin method of Weigert, ordinary hæmatoxylin, hæmatoxylin and carminate of soda, carminate of soda alone, and a modified method of hæmatoxylin-staining by Dr. George R. Elliott (as yet unpublished). By means of these reagents the following findings were elicited:

In the cervical region, on account of the terminal tubercular myelitis, sections hardened in Müller's fluid and prepared for hæmatoxylin were very unsatisfactory, but degeneration in the crossed and direct pyramidal tracts with almost complete destruction of the anterior horns could be made out.

The third dorsal segment showed: *a.* Sclerosis of the crossed pyramidal tracts. *b.* Slight sclerosis of the ascending cerebellar tract. *c.* Diffusely distributed dilated bloodvessels, some with very much thickened walls. *d.* Extensive atrophy of the cells of the anterior horns. The cells are small and shrivelled-looking and their process stunted.

The eighth dorsal segment showed: *a.* Sclerosis of the crossed pyramidal tracts. *b.* Slight sclerosis of the ascending cerebellar tract. *c.* Bloodvessels with thickened walls, chiefly in the vicinity of the central gray commissure and in the pia mater.

The twelfth dorsal segment showed: *a.* Sclerosis of the crossed pyramidal tracts. *b.* Similar vascular condition to that higher up. *c.* Considerable cell-atrophy, most marked in the antero-internal and median groups.

The third lumbar segment showed: In addition to slight diffuse thickening and dilatation of the bloodvessels, there is a moderate degree of atrophy of the cells of the antero-internal and median groups of one side and the median of the other; slight degeneration of the crossed pyramidal tracts.

The fifth lumbar segment showed: Slight atrophy of the median groups of the anterior horn cells of both sides.

The ninth dorsal segment showed: *a.* Sclerosis of crossed pyramidal tracts. *b.* The bloodvessels much thickened, in places diffusely distributed through the cord and pia mater. Some of the bloodvessels are markedly dilated. *c.* At the extreme posterior part of the lateral column adjoining the pyramidal tract on one side is the site of old hemorrhage about the size of a pea. *d.* Some scattered cells in the anterior columns seem very much diminished in size without nuclei and without processes. *e.* In the anterior nerve-roots are dilated bloodvessels, together with slight increase of neuroglia-tissue.

At this level of the cord is seen a very interesting artificial displacement of the vesicular column of Clarke, which is pushed over to the opposite side, causing it to lie in juxtaposition with its fellow.¹ The remaining segments of the dorsal cord show conditions similar to those that have been described.

A section of the medulla at the level of the upper middle third of the twelfth nerve nucleus shows a considerable disappearance of the cells of the nucleus of this nerve, while many of the cells that remain are contracted, granular, without nuclei or processes, these changes being confined principally to the intraventricular portion of the nucleus. The outline of the nucleus would seem to be moderately preserved. Many of the fibres of the twelfth nerve in their course through the medulla show well-defined evidences of degeneration. In the substance of the nucleus there are many dilated bloodvessels and the dilatation of the perivascular spaces is particularly noticeable. Sections of the pons appear to present an entirely normal appearance.

Clinical summary of Case II.: Male, aged forty-eight years; onset of symptoms in October, 1893; temporary difficulty and indistinctness of speech and weakness in the left arm; the former gradually disappeared and the latter became worse gradually. Speech-difficulty recurred very soon and became permanent about December, 1893. Bulbar speech. Weakness of legs; difficulty in walking; increasing atrophy of left hand and arm. Mentally normal; sphincters physiological. Partial paralysis of the muscles of the left arm, forearm, and hand; hand-muscles most atrophied. No contractures. Tendon-reflexes greatly exaggerated. Diminution of electrical irritability in atrophied muscles. No sensory disturbances. Legs weak, left more so than right, and beginning atrophic changes. No difficulty in swallowing; no affection of the special senses. Course of the disease progressive: at first rather slowly, but later more rapidly, and for several days before death there were high temperature and evidences of some specific infection. With the excep-

¹ This artefact is fully described in the *Neurologisches Centralblatt*, No. 22, 1895.

tion of just previous to death, there had been no marked trouble with speech or swallowing. A peculiar symptom, spasmodic tasting, smacking movements of lips and tongue, quite involuntary and beyond control.

Summary of morbid changes: 1. A marked sclerosis of the crossed pyramidal tracts, moderate degeneration of the direct. 2. Marked atrophy of the cells of the anterior horns of the spinal cord. 3. Markedly dilated and thickened bloodvessels, rather diffusely distributed. 4. Atrophic changes in the cells of the twelfth nerve nucleus. 5. Destructive myelitis of the cervical region, tuberculous in character. 6. Hemorrhage, of ancient date, in the dorsal region.

The belief that the affection of the gray matter is secondary or deuteropathic in amyotrophic lateral sclerosis is more in keeping with the basic anatomical units of the nervous system, the neuron, than is the view taken by Leyden and Gowers. We know that the centre for nutrition of the neuron is the cell-body of the neuron, and that parts most remote from the cell-body are the first to show degeneration when the nutrition of the centre is affected. In the cases such as we have reported, and particularly in Case I., the slowly proceeding vascular degeneration caused, first, lack of nutrition in the perivascular lymph-spaces, and, as it is in these spaces that the ramifications of the end-brushes take place, it is easily conceivable that the degeneration will extend from such loci and gradually creep up the collaterals and axis-cylinder processes until the entire neuron or neurodendron is involved. This can be taken as the procedure for the changes in the principal neuron; *i. e.*, the one extending from the cortex to the anterior horns. The same vascular and perivascular changes acting upon the dendrites of the cell-body of the secondary neuron, and upon the cell-body itself, will have their deleterious results manifested in the terminal arborizations of the neuraxon, *viz.*, in the muscles, and the manifestation of it then will be muscular atrophy.

It is not only possible, but very probable, that in many cases of amyotrophic lateral sclerosis in which the lesion of the pyramidal tracts could be traced from the cortex to the periphery, such cases as were enumerated in the beginning of the paper, the degeneration may have had its starting-point in the ganglionic cells of the cortex which are the beginnings of the fibres of the pyramidal tracts, and extended from there downward; but the fact that the degeneration may occur in that way does not invalidate what has been said about the probable way in which the lesion developed in these cases. That is, it cannot be regarded that the former is the only way that the degeneration may take place, for even one thorough observation, which showed that the lesion in the pyramidal tracts did not extend above the pons, would prove the falseness of such a contention. That there have been plenty of such cases everyone must admit. In Case I., reported herewith, the most accurate methods of investigation were used; for instance, the method of

Marchi, which reveals with unerring accuracy any degenerating fibres which are present; but in this case the reaction of the tissues above the pons to the stain was that of normal fibres.

The etiology of the disease cannot be said to be directly contributed to by these two cases. Indirectly, however, they furnish us with much information of inferential value. When we have succeeded in making out a sequence of events to our entire satisfaction, when we know all about it, and the laws involved are so familiar that we seem to understand how such a beginning must have been followed by just such an end, we shall then be justified in applying such acquired knowledge as an explanatory principle to the etiology of the disease, thus determining its cause or causes.

The depravity of the vascular system was, to my mind, the main factor in the causation of the disease in the neuron. If this be granted, two questions only remain to be considered: the first concerns itself with the cause of the disease of the vessels, the second with the *raison d'être* of the selection of its deleterious consequences upon the neuron. The discussion of these two questions would involve the consideration of the causes of vascular degeneration as they occur all over the body, and, in addition, a theory of the causation of those organic nervous diseases which are not congenital (a group of diseases which, in the opinion of the writer, is steadily becoming more limited), such as the well-known theory recently resuscitated by Edinger. Into such a discussion I prefer not to go in this connection.

The significance of the tubercle-bacilli in the second case is not an easy matter to determine.¹ Whereas, the probability is that the tuberculous infection was a somewhat recent one and engrafted on the other disease, predisposed to by the perverted nutrition of the part, yet the opinion might laudably be advanced that the tubercle-bacilli played a more important rôle in the causation of the disease, but still no proof could be brought forward to support such a hypothesis.

From the point of view of symptomatology there are but two or three points to arrest our attention and call for discussion, and of these by far the most striking and uncommon one was the waves of spasmodic smiling and laughter in the first patient, and the involuntary chewing, quiet "smacking" movements in the second. Involuntary and uncontrollable expression of the emotions, either by laughing or crying, has been noticed and described in connection with several organic diseases of the central nervous system, particularly with hemiplegia of cerebral origin and with multiple sclerosis, but it has rarely been noticed in connection with amyotrophic lateral sclerosis, except by Marie (*Leçons de*

¹ The myelitis of tubercular origin will be considered more extensively in a subsequent communication.

Maladie de Moelle). Its explanation is a simple one, and its mechanism is a light or deep contraction of the inferior facial muscles supplied by the seventh nerve in the case of laughing, and of the fifth nerve in the case of chewing. We must conceive of a loss of a proper hold or tenacity of the nuclei of the fifth and seventh nerves on their peripheral belongings, or an excitation of these nuclei which causes a spasmodic movement in the mimic or masticating muscles, which passes off as soon as the nuclei readjust themselves. I have seen a similar phenomenon occur in two cases of bulbar paralysis, and, indeed, in one of them the spasmodic and impertinent attacks of uncontrollable laughter were the first symptom of the disease, which, later, ran a course significant of bulbar softening following a thrombosis.

The pain in the back of the head and neck and excessive rigidity and stiffness of the neck in Case I. were very striking, and considering the fact that it was asserted by the patient that they were initial symptoms, they at once suggested a diagnosis of pachymeningitis cervicalis or meningo-myelitis, but the presence of other symptoms, particularly the bulbar, and the absence of sensory disturbances quickly served to eliminate this suspicion.

The manner of onset in the second case is an extremely uncommon one and not devoid of interest, inasmuch as it suggests that the first manifestations of the disease were in the medulla, and the fact that the speech-disturbance was temporary and repeated until it became secondary would lead us to believe that the actual process was a vascular one, the first attack and each succeeding one coinciding with some local ischemia secondary to the diseased bloodvessels. We say ischemia, because no evidences of slight hemorrhages or blocking up of vessels were found on histological examination, conditions which one might be led to suspect from the development of the symptoms; yet diseased and thickened bloodvessels were very conspicuous.